DELHI PHARMACEUTICAL SCIENCES & RESEARCH UNIVERSITY

(Incorporating DIPSAR as Constituent College as per DPSRU Act)

Proposal/ Synopsis

For

Doctor of Philosophy

Govt. of NCT of Delhi

Pushp Vihar, Sector-III, M.B.Road,

New Delhi-110017

Website: www.dpsru.edu.in

(Approved by UGC under section 2f of UGC Act)

DELHI PHARMACEUTICAL SCIENCES & RESEARCH UNIVERSITY

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Registration No: 36/Ph.D/DPSRU/2019

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Proposed Project Title: "Study of Effects of Transdermal Drug Delivery of Succinylcholine in Myofascial Pain Syndrome and its Comparison with Conventional Treatment"

(Name ad Signature of the Research Scholar)

Countersignature of Supervisor

of. Ramesh K. Goyal
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Study of Effects of Transdermal Drug Delivery of Succinylcholine in Myofascial Pain Syndrome and its Comparison with Conventional Treatment

Background

Skeletal muscle pain is prevalent globally and occurs due to long or unusual sitting and working hours. About 10% of such individuals experience back pain as a part of a neurologic syndrome. Of these, 5% have specific identifiable causes, while remaining 85% have no specific identifiable etiology quoted by *Gupta L et.al.* [8]

Myofascial pain syndrome is also one of the problems, a pain condition characterized by the presence of active trigger points, pain and spasm. Chronic MFPS can lead to recurrent muscle spasms. Spasms in these muscles can be a result of an injury or they may develop over time because of over stress, arthritic / degenerative changes in musculoskeletal system stated by *Fernandez C.* [7]

Myofacial pain related spasms may occur when a muscle is

- overused
- tired
- previously injured
- Strained
- overstretched or
- Held in the same position for a prolonged period of time *(Postural)*.

Consequently, the muscle lacks in energy and fluid and becomes hyper excitable, resulting in a forceful contraction. This spasm may involve part of a muscle, the whole muscle, or even adjacent muscles. [1, 2, 3 &5]

Pavkovich R. 2015 reported Excessive acetylcholine release affects formation of the taut band causing a palpable nodule in the muscle causing localized hypoxia of the muscle caused by increased energy consumption and decreased energy supply, creating an "energy crisis" within the muscle, and the release of energy consuming *localized contracture* leads to tissue ischemia. This situation can be positively affected by eliciting the local twitch response. Such contractures can lead to recurrent spasms which may be a cause of localized fiber damage. [10, 11]

Myofascial trigger points (MTrPs) are considered as hyperirritable spots in taut bands of skeletal muscles, which are composed of numerous "contraction knots" in muscle fibers. The existence of active MTrPs causes a series of clinical pain-related complaints owing to the shortening of the muscle fiber and pressure on nearby nerves or veins due to these contraction

knots. Therefore, the inactivation or elimination of MTrPs by various interventions may relieve chronic myofascial pain reported by *Li L. 2019.* [15]

Shah JP, 2015 also versed that to identify TrPs, according to Trvel and Simon's and to consider possible clinical diagnostic criteria in the light of the pathophysiology of MTrPs.[15] Simon D. in 1999 and 2010 upgraded the criteria which was used to diagnose for so many years was descriptive due to which pathogenic elements in the nodule remained unknown Nature of Trigger Points three recently identified objective confirmatory findings of MTrPs include: the electromyographic recording and ultrasound imaging of local twitch responses, the spontaneous electrical activity of multiple active loci in the MTrP, and biopsies of MTrPs that show contraction knots and giant round muscle fibers. Many of the clinical characteristics of MTrPs can be accounted for by their pathophysiology. Conclusion: The endplate dysfunction characteristic of MTrPs involves both the nerve terminal and the postjunctional muscle fiber. This relationship identifies MTrPs as a neuromuscular disease. [13, 14]

- Several interventions are proposed for treating trigger points, like US therapy, LASER, Ischaemic compression, dry needling which is being one of the most commonly used by therapists, *Fernández C, 2019* [7].
- Studies have demonstrated that Succinylcholine is a quaternary skeletal muscle relaxant usually used in the form of its bromide, chloride, or iodide. Succinylcholine is indicated as an adjunct to general anesthesia, to facilitate tracheal intubation, and to provide skeletal muscle relaxation during surgery or mechanical ventilation. It is a depolarizing skeletal muscle relaxant, acting in about 30 seconds and with duration of effect averaging three to five minutes.

Objective

The Objective of the study was to develop and evaluate the effects of the succinylcholine nano formulation for the treatment of MFPS and compare it with other conventional treatments including dry needling.

Aims

1. Development of the nano formulation of Succinylcholine drug and its evaluation with respect to Physical and Chemical properties.

2. To conduct a preliminary study of the developed formulation to evaluate its effects on pain.

3. To develop a reliable and valid questionnaire for spasm developed due to Myofascial Pain Syndrome (MFPS).

4. To conduct a clinical study to evaluate the effect of developed nano formulation of succinylcholine and to compare its effects with dry needling and conventional physiotherapy treatment.

Research Methodology (Proposed)

The study will be conducted in three phases

Phase 1: Development of the nano formulation of Succinylcholine drug and its evaluation with respect to Physical and Chemical properties.

Phase 2: Development of clinical methods for evaluation of the muscle spasm and a Pilot study of the developed formulation to evaluate its efficacy on pain.

Phase 3: Extension of the study to the statistically appropriate number of subjects.

Sample Size: Sample size will be calculated using below formula

$$n = \frac{2\sigma^2 (Z_{\alpha/2} + Z_{\beta})^2}{(\mu_t - \mu_c)^2}$$

$Z_{\alpha/2}$: Z value from the standard normal distribution, 1.96
Z_{β}: Z value from the standard normal distribution, 1.282
$\mu_t - \mu_c$: true mean difference
σ: population standard deviation, assumed as $\sigma = \sigma_t = \sigma_c$

Inclusion Criteria:

- Patients with symptoms of MFPS according to Travel and Simon's criteria
- Patients who'll provide their consent to participate in the study

Exclusion Criteria:

Major associated co- morbidities in patients like

- Severe uncontrolled diabetes
- Severe neurological problems
- Patients with severe renal disease
- known case of psychological and psychiatric conditions
- patients with Cardiovascular problems

Duration of the treatment

- 3 days a week (following the set protocols of the intervention)

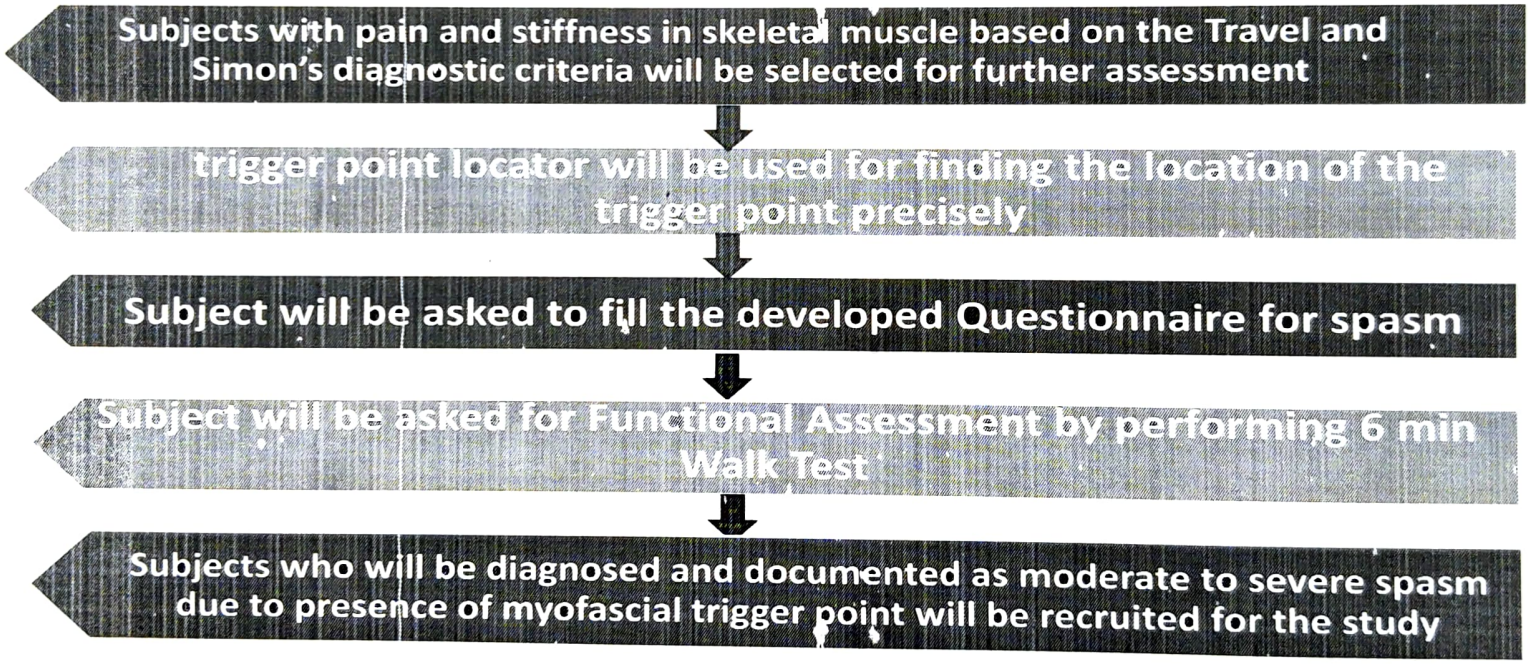
For subjects receiving phonophoresis with the formulated drug

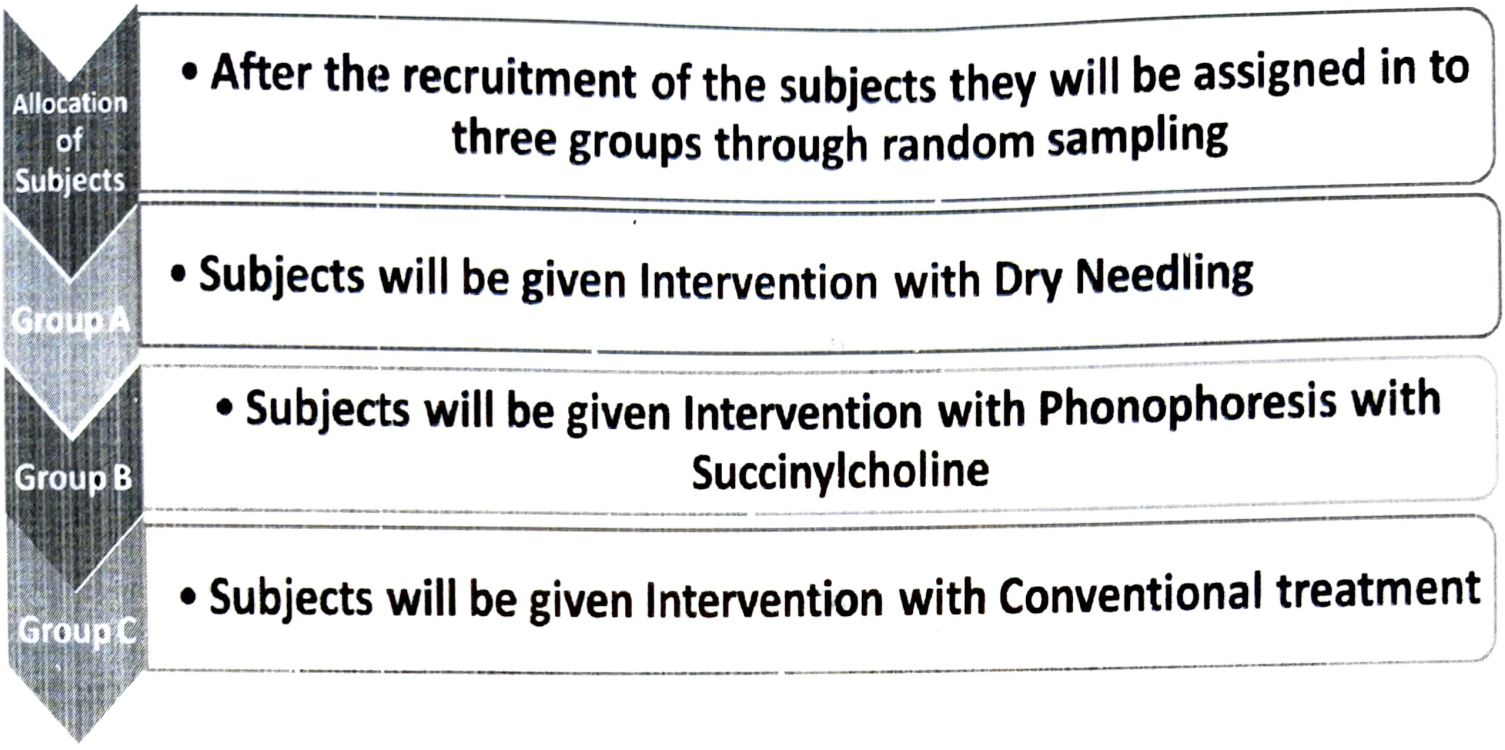
- Intensity of US Therapy: 1.2 W/cm^2
- Frequency: 1 MHz
- Mode: Continuous
- Dosage of the drug: 25 % (25 mg in 24 hours)

Data Collection Tools

1. **Pain:** Threshold/ Tolerance- By using Algometer
   Severity- VAS
2. **Spasm:** using a standardized tool (that would be developed for this purpose)
3. **Myofascial trigger point diagnosis:** Based on the criteria given by Travel and Simon Myofascial Trigger Point Locator [14]

Proposed procedure


Subjects with pain and stiffness in skeletal muscle based on the Travel and Simon's diagnostic criteria will be selected for further assessment
trigger point locator will be used for finding the location of the trigger point precisely
Subject will be asked to fill the developed Questionnaire for spasm
Subject will be asked for Functional Assessment by performing 6 min Walk Test
Subjects who will be diagnosed and documented as moderate to severe spasm due to presence of myofascial trigger point will be recruited for the study


Allocation of Subjects
• After the recruitment of the subjects they will be assigned in to three groups through random sampling
Group A
• Subjects will be given Intervention with Dry Needling
Group B
• Subjects will be given Intervention with Phonophoresis with Succinylcholine
Group C
• Subjects will be given Intervention with Conventional treatment

Plan of Work

Phase I: Literature survey and finding of the gap

Phase II: Review for the study with gap defined will be sent for the publication and data will be collected.

Phase III: Statistical analysis of the collected data and results will be compiled.

Novelty

As per our understanding phonophoresis using succinylcholine is a novel method for treating Myofascial Pain Syndrome if applied on MTrP

Annexure I

Informed Consent Form

प्रतिभागी सूचना पत्रक

Consent to Participation in Research/ Study

Title of the Research/ Study: **Efficacy of Transdermal Drug Delivery of Succinylcholine in Myofascial Pain Syndrome in Comparison with Dry Needling and Conventional Physiotherapy Treatment- A Randomized Controlled Trial**

Investigator's Name: Shilpa Jain

I have read and understood the information provided about this research project.

- I have had an opportunity to ask questions and to have them answered.
- I understand that the data recorded from the testing sessions will be stored on computer for analysis.
- I understand that I may withdraw myself or any information that I have provided for this project at any time prior to completion of data collection, without being disadvantaged in any way.
- If I withdraw, I understand that all relevant data, or parts there of, will be destroyed
- I agree to take part in this research.
- I have no injuries or medical conditions that may affect my ability to do balance training or to perform resistance training..

Signature of the subject: .....

Name of the subject: .....

Date: .....

Contact Details:

Address:

Ph:

E-mail:

Subject Information Sheet

Contact person:

Shilpa Jain , PhD Scholar, Delhi Pharmaceutical Sciences and Research University, New Delhi .

Ph: 7060443388, E-mail: shilpa.jain36@gmail.com

Project Title: **Efficacy of Transdermal Drug Delivery of Succinylcholine in Myofascial Pain Syndrome in Comparison with Dry Needling and Conventional Physiotherapy Treatment- A Randomized Controlled Trial**

Location

Testing and treatment will be conducted at the School of Physiotherapy, DPSRU and various Physiotherapy Clinics of Delhi, NCR and Haryana. Physician evaluation prior to participation will be conducted by the Medical Officer, DPSRU and other Physician available at various settings.

Invitation

You are invited to take part in this study, which is being carried out as PhD research project in the School of Physiotherapy, DPSRU. Your participation in this study is voluntary. You are free to withdraw consent and discontinue participation at any time without influencing any present and/or future involvement with DPSRU.

Your consent to participate in this research will be indicated by your signing and dating the consent form. Signing the consent form indicates that you have freely given your consent to participate, and that there has been no coercion or inducement to participate.

What is the purpose of the study?

To compare the effectiveness of targeted topical formulation of succiylcholine with dry needling

Selection of Subjects

Volunteers that meet the criteria will be included in this study.

These criteria include:

Participants who satisfy the following criteria will be recruited to participate

1) Presence of myofascial trigger point as per diagnostic criteria by Travel and Simon Presence of symptoms
2) Presence of the trigger point as located by the trigger point locator
3) Tenderness and stiffness in the periphery of 25 cm^2 of the nodule found

What happens in the study?

You will undergo a detailed assessment for **presence of trigger point and its evaluation**

After that you may be allocated to either of one group of the management protocols. The training will be for one week with 3 sessions in the week on alternate days. After that post intervention training assessment for **presence of trigger point and its evaluation** will be repeated.

What are the discomforts and risks?

There is possible risk of mild to moderate soreness after needling or itching after topical application of the formulation. This is however an equivalent risks to normal participation in active exercises or conventional treatment. You would be given free care at the health centre and/or physiotherapy clinic, if any possibility of discomfort occurs during the course of study.

What are the benefits?

You will be given free access to state of the art Physiotherapy and General OPD of DPSRU and the concerned settings during the course of the study. You will gain detailed information on your

pain which occurs repeatedly. This information may better aid you in planning future exercise programmes, health and fitness.

How is my privacy protected?

The identity of individuals will not be made available to any other source, and any information published elsewhere will have subject identities concealed.

Costs of Participating

The only cost to you the subject is approximately one hour of your time on the day you attend the centres/ hospital testing and treatment.

Subject Concerns

Any concerns regarding the nature of this project should be notified in the first instance to the Project Supervisor. Concerns regarding the conduct of the research should be notified to the Institutional Human Research Ethics Committee of DPSRU.

Signature of the research scholar

प्रतिभागी सूचना पत्रक

सम्पर्क सूत्र:
शिल्पा जैन, पीएचडी स्कॉलर, दिल्ली फार्मासेक्टिकल साइंराज एंड रिसर्च यूनिवर्सिटी, नई दिल्ली।
Ph: 7060443388 ई-मेल: shilpa.jain36@gmail.com

अनुसंधान/ अध्ययन का शीर्षक: ड्राई नीडलिंग और पारंपरिक फिजियोथेरेपी उपचार के साथ तुलना में मायोफेशियल दर्द सिंड्रोम में Succinylcholine के ट्रांसडर्मल ड्रग डिलीवरी की प्रभावकारिता - एक यादृच्छिक नियंत्रित परीक्षण

स्थान
परीक्षण और उपचार दिल्ली, एनसीआर और हरियाणा के फिजियोथेरेपी, डीपीएसआरयू और विभिन्न फिजियोथेरेपी क्लीनिक के स्कूल में आयोजित किया जाएगा। भागीदारी से पहले चिकित्सक का मूल्यांकन चिकित्सा अधिकारी, डीपीएसआरयू और अन्य चिकित्सकों द्वारा विभिन्न सेटिंग्स में उपलब्ध कराया जाएगा।

निमंत्रण
आपको इस अध्ययन में भाग लेने के लिए आमंत्रित किया गया है, जिसे स्कूल ऑफ फिजियोथेरेपी, DPSRU में पीएचडी अनुसंधान परियोजना के रूप में किया जा रहा है। इस अध्ययन में आपकी भागीदारी स्वैच्छिक है। आप DPSRU के साथ किसी भी वर्तमान और / या भविष्य की भागीदारी को प्रभावित किए बिना किसी भी समय सहमति को वापस लेने और बंद करने के लिए स्वतंत्र हैं।

इस शोध में भाग लेने के लिए आपकी सहमति पर हस्ताक्षर करने और सहमति फॉर्म को डेटिंग करने का संकेत दिया जाएगा। सहमति फॉर्म पर हस्ताक्षर करना यह दर्शाता है कि आपने भाग लेने के लिए स्वतंत्र रूप से अपनी सहमति दे दी है, और यह कि भाग लेने के लिए कोई ज़बरदस्ती या आनाकानी नहीं की गई है।

अध्ययन का उद्देश्य क्या है?
ड्राई नीडलिंग के साथ succiylcholine के लक्षित सामयिक सूत्रीकरण की प्रभावशीलता की तुलना करने के लिए

प्रतिभागी का चयन

मानदंडों को पूरा करने वाले स्वयंसेवकों को इस अध्ययन में शामिल किया जाएगा।

इन मानदंडों में शामिल हैं:

निम्नलिखित मानदंडों को पूरा करने वाले प्रतिभागियों को भाग लेने के लिए भर्ती किया जाएगा
1) Travel and Simon के लक्षणों के अनुसार नैदानिक मानदंडों के अनुसार मायोफेशियल ट्रिगर बिंदु की उपस्थिति
2) ट्रिगर बिंदु लोकेटर द्वारा स्थित ट्रिगर बिंदु की उपस्थिति
3) पाए जाने वाले नोड्यूल के 25 सेमी 2 की परिधि में कठोरता, दबाने पर दर्द होना

अध्ययन में क्या होता है?

आप ट्रिगर बिंदु की उपस्थिति और इसके मूल्यांकन के लिए एक विस्तृत मूल्यांकन से गुजरेंगे, उसके बाद आपको प्रबंधन प्रोटोकॉल के किसी एक समूह को आवंटित किया जा सकता है। प्रशिक्षण वैकल्पिक दिनों में सप्ताह में 3 सत्रों के साथ तीन सप्ताह के लिए होगा। ट्रिगर प्वाइंट की उपस्थिति और उसके मूल्यांकन के बाद हस्तक्षेप के बाद प्रशिक्षण मूल्यांकन दोहराया जाएगा।

असुविधाएँ और जोखिम क्या हैं?

सूत्रीकरण के सामयिक अनुप्रयोग के बाद खुजली जैसे या सुई लगने के बाद हल्के से मध्यम दर्द का खतरा होता है। हालांकि यह सक्रिय व्यायाम या पारंपरिक उपचार में सामान्य भागीदारी के लिए एक समान जोखिम है। यदि अध्ययन के दौरान कोई असुविधा होती है, तो आपको स्वास्थ्य केंद्र और / या फिजियोथेरेपी क्लिनिक में मुफ्त देखभाल दी जाएगी।

असुविधाएँ और जोखिम क्या हैं?

सूत्रीकरण के सामयिक अनुप्रयोग के बाद सुई या खुजली के बाद हल्के से मध्यम खराश का खतरा होता है। हालांकि यह सक्रिय व्यायाम या पारंपरिक उपचार में सामान्य भागीदारी के लिए एक समान जोखिम है। यदि अध्ययन के दौरान कोई असुविधा होती है, तो आपको स्वास्थ्य केंद्र और / या फिजियोथेरेपी क्लिनिक में मुफ्त देखभाल दी जाएगी।

अध्ययन के क्या लाभ हैं?

आपको अध्ययन के दौरान आर्ट फ़िजियोथेरेपी की स्थिति और डीपीएसआरयू के जनरल ओपीडी और संबंधित सेटिंग्स तक मुफ्त पहुंच दी जाएगी। आप अपने दर्द पर विस्तृत जानकारी प्राप्त करेंगे जो बार-बार होता है। यह जानकारी आपको भविष्य के व्यायाम कार्यक्रमों, स्वास्थ्य और फिटनेस की योजना बनाने में बेहतर सहायता कर सकती है।

मेरी गोपनीयता कैसे सुरक्षित है?

व्यक्तियों की पहचान किसी अन्य स्रोत को उपलब्ध नहीं कराई जाएगी, और कहीं भी प्रकाशित किसी भी जानकारी को विषय पहचान छुपाया जाएगा।

भाग लेने की लागत

जिस दिन आप केंद्र / अस्पताल परीक्षण और उपचार में भाग लेंगे उस दिन आपके लिए केवल एक घंटे का समय लगभग एक घंटे है।

प्रतिभागी की चिंता

इस परियोजना की प्रकृति के बारे में कोई भी चिंता पहली बार में परियोजना पर्यवेक्षक को सूचित की जानी चाहिए। शोध के संचालन के संबंध में DPSRU की संस्थागत मानव अनुसंधान आचार समिति को सूचित किया जाना चाहिए।

अनुसंधान विद्वान का हस्ताक्षर

अनुसंधान में भागीदारी के लिए सहमति

अनुसंधान/ अध्ययन का शीर्षक : ड्राई नीडलिंग और पारंपरिक फिजियोथेरेपी उपचार के साथ तुलना में मायोफेशियल दर्द सिंड्रोम में Succinylcholine के ट्रांसडर्मल ड्रग डिलीवरी की प्रभावकारिता - एक यादृच्छिक नियंत्रित परीक्षण

अन्वेषक का नाम: शिल्पा जैन

मैंने इस शोध परियोजना के बारे में दी गई जानकारी को पढ़ा और समझा है।

- मुझे सवाल पूछने और उन्हें जवाब देने का अवसर मिला है।
- मैं समझता/ समझती हूं कि परीक्षण सत्रों से रिकॉर्ड किए गए डेटा को विश्लेषण के लिए कंप्यूटर पर संग्रहीत किया जाएगा।
- मैं समझता/ समझती हूं कि मैं किसी भी समय डेटा संग्रह के पूरा होने से पहले किसी भी समय इस परियोजना के लिए अपने द्वारा प्रदान की गई किसी भी जानकारी को स्वयं या किसी भी तरह से बिना किसी नुकसान के वापस ले सकता हूं।
- यदि मैं सहमति वापस लेता/ लेती हूं, तो मैं समझता/ समझती हूं कि सभी प्रासंगिक डेटा, या वहां के कुछ हिस्सों को नष्ट कर दिया जाएगा
- मैं इस शोध में भाग लेने के लिए सहमत हूं।
- मुझे कोई चोट या चिकित्सा की स्थिति नहीं है जो संतुलन प्रशिक्षण करने या प्रतिरोध प्रशिक्षण करने की मेरी क्षमता को प्रभावित कर सकती है।

प्रतिभागी का हस्ताक्षर: .....

प्रतिभागी का नाम: .....

तारीख: .....

सम्पर्क करने का विवरण: .....

पता: .....

Ph: .....

ई मेल: .....

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